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REMARKS

Claims 1-14 and 18-43 are pending in the present application. Claims 1, 9, and 13 have been amended. Support for the amendments is found throughout the specification. No new matter has been added by virtue of these amendments and their entry is respectfully requested. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

Claim Rejections Under 35 U.S.C. § 112.

Claims 1 and 9 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response, Applicants have amended claim 1 to remove the term "analyzing" and replacing the term with "detecting." Applicants have also amended claim 9 to substitute the term "marker" with "protein" so as to provide the correct antecedent basis. These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 U.S.C. § 103.

Claims 1, 9-11 and 13-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,235,713 B1 (filed Aug 1997; PTO 892) in view of U.S. Patent No. 5,874,290 (Feb 1999; PTO 892) and Hamel et al (*Acta Neurochirurgica* 142:113-138, 2000; PTO 892, Wesseling et al (*J. Neurosurg.* 81(6):902-9, Dec 1994; PTO 892) and Amalfitano et al., (*Cancer Genet Cytogenet* 116:6-9, 2000; PTO 892).).

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Applicants respectfully disagree and traverse the rejection.

Applicants reiterate that the '290 patent does not teach or disclose that VEGF-D is over-expressed in brain tumors. The material used in '290 is fetal brain tissue and not glioblastomas. Further, '209 does not teach or disclose that the molecule detected in fetal brain tissue is VEGF-D. VEGF was detected in some brain tumors but the '290 patent does not teach or disclose detection and over-expression of VEGF-D as a diagnostic marker of brain tumors isolated from human brain tissue samples. As stated in previous responses, the '290 patent utilized established cell lines for detection of the D2-2 gene. (See, for example, column 43, lines 49-62). Applicants submit that fetal brain tissue is not a tumor as suggested by the Examiner and consequently cannot be used as a tool to diagnose brain tumors.

As the Examiner states, the references do not teach a method of detecting cancer in a brain tissue sample. The '713 patent does not teach or suggest that full-length native VEGF-D is detected in brain tissue samples. Hamel *et al* do not teach or disclose the detection of full-length native VEGF-D in glioblastomas detected in brain tissue samples. Wesseling *et al* do not teach or disclose the detection of full-length native VEGF-D in brain tissue samples or of detection of VEGF-D. Amalfitano *et al.*, do not teach the detection of full-length native VEGF-D in brain tissue samples. None of the references alone or in combination teach or disclose the detection of full-length native VEGF-D in human brain tissue samples containing glioblastomas.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claims 12 and 18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,235,713 B1 (of record, filed Aug 1997; PTO 892) in view of U.S. Patent No. 5,874,290 (of record, Feb 1999; PTO 892) Hamel *et al* (*Acta Neurochirurgica* 142:113-138, 2000; PTO 892, Wesseling *et al* (*J. Neurosurg.* 81(6):902-9, Dec 1994; PTO 892) as applied to claims

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1, 9-11 and 13-14 and further in view of Achen *et al* (of record, Eur. J. Biochem. 267:2505-2515, May 2000; PTO 1449).

Applicants respectfully traverse.

As the Examiner has stated, that the instant invention differs in that the method for detecting glioblastoma multiforme wherein the monoclonal antibody binds to the homology domain of human VEGF-D.

As discussed, the references do not teach VEGF-D. There is no teaching in the references, alone or in combination that show that the antibody binds to different VEGF types binds to the VEGF-D detected in the human glioblastomas of the instant invention. Arguments regarding the combined teachings of '713 and '290 and Hamel have been discussed *supra*, and for the sake of brevity will not be repeated here. Achen *et al*, standing alone or in combination teach the detection of a native protein VEGF-D homology domain in brain cancer. None of the references teach the detection of VEGF-D in the brain nor, was the form of VEGF-D in the brain known prior to applicants invention.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Applicants respectfully request entry of the foregoing remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1, 9, 10 and 12-18 define patentable subject matter and is in condition for allowance. Accordingly, Applicant respectfully requests allowance of these claims.

Applicants have made every effort to present claims which distinguish over the cited art, and it is believed that all claims are now in condition for allowance. However, Applicants

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request that the Examiner call the undersigned (direct line 561-671-3666) if anything further is required by the Examiner prior to issuance of a Notice of Allowance for all claims.

This response is being filed with a petition for a one month extension and appropriate fees. Although, Applicants believe that no further extensions of time or fees are due, please consider this submission as a petition for any retroactive extension of time needed. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for a one month retroactive extension of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing, or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

AKERMAN SENTERFITT



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